REMARKS

Claims 1-21 are currently pending in the application. Only claims 1 and 12 are in independent form.

The disclosure is objected to because of informalities on page 2, line 24. Appropriate corrections of these informalities have been made herewith. Reconsideration of the objection is respectfully requested.

Claims 1-21 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention.

With regard to claims 1-11, the Office Action states that "the activity or concentration" and "the quality of....label" lack antecedent basis. The claims have been amended to provide proper antecedent basis for these phrases and reconsideration of the rejection is respectfully requested.

In claim 2, the Office Action states that "pin-like" or "cone-like" are vague as to what shapes are contemplated by Applicants. In order to further prosecution, the claim has been amended, without prejudice, to remove "like" from the claim. Reconsideration of the rejection is respectfully requested.

In claims 12-21, the Office Action states that "the activity or concentration" and the "quality of...label" lack antecedent basis. The claims have been amended to provide proper antecedent basis for these phrases and reconsideration of the rejection is respectfully requested.

The Office Action states that in claim 13, "pin-like" and "cone-like" are vague as to what shapes are contemplated by Applicants. The claim has been amended, without

prejudice, in order to further prosecution and reconsideration of the rejection is respectfully requested.

Claims 1-11 stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Eibl et al. patent. Reconsideration of the rejection under 35 U.S.C. § 102(b), as anticipated by the Eibl et al. patent, as applied to the claims is respectfully requested. Anticipation has always been held to require absolute identity in structure between the claimed structure and a structure disclosed in a single reference.

In Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986) it was stated: "For prior art to anticipate under §102 it has to meet every element of the claimed invention."

In Richardson v. Suzuki Motor Co., Ltd., 868 F.2d 1226, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989) it was stated: "Every element of the claimed invention must be literally present, arranged as in the claim."

The Office Action states that the Eibl et al. patent discloses elongated elements such as "platelets" or pins, which are secured to a holding band in a carrier and that are insertable into the recesses of a microtiter plate containing samples to be assayed. Further, the Office Action states that various competitive assay formats are taught using an antigen or antibody bound to the elements and a labeled antigen or antibody added to the sample. Therefore, the Office Action concludes that the Eibl et al. patent teaches the carrier for the avoidance of complicated separating and washing procedures as are found in prior art assays performed with coated vessels, such as tubes. It is undisputed that the Eibl et al. patent discloses the use of elements that are secured to a holding band in a carrier that is insertable into the recesses of a microtiter plate containing samples to be assayed. However, when read more specifically, the Eibl et al. patent teaches an assay that utilizes "a solution of the radioactively labeled antibody is added to the sample to be examined for a content of antigen or antibody, and then a solid carrier loaded with unlabeled antigen is contacted with the sample liquid, whereupon

after washing of the carrier, the radioactivity of the carrier is measured." This is specifically set forth in column 2, lines 28-33, of the Eibl et al. patent. In other words, the Eibl et al. patent teaches an assay kit, but still requires a washing step in order to measure the radioactivity of the carrier. While the Eibl et al. patent discloses an assay kit with a decreased amount of steps required for performing the assay, it still requires washing procedures to be used in order for the assay to perform properly. This is in contradistinction with the method of the presently pending claims, which instead do not require a washing step. It was previously thought by those of skill in the art that washing was required in order to stop the reaction; i.e., stopping the biological activity of the bioactive molecule and also to remove any unbound ligand. The presently pending claims, therefore, are beneficial over the prior art in that they are able to remove the washing step and thereby simplify the assaying procedure. Since the Eibl et al. patent does not disclose the method of the presently pending claims, the claims are patentable over the Eibl et al. patent and reconsideration of the rejection is respectfully requested.

Claims 12, 14-18, and 20-21 stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Behnke et al. patent. Reconsideration of the rejection under 35 U.S.C. § 102(b), as anticipated by the Behnke et al. patent, as applied to the claims is respectfully requested. Anticipation has always been held to require absolute identity in structure between the claimed structure and a structure disclosed in a single reference.

In Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986) it was stated: "For prior art to anticipate under §102 it has to meet every element of the claimed invention."

In Richardson v. Suzuki Motor Co., Ltd., 868 F.2d 1226, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989) it was stated: "Every element of the claimed invention must be literally present, arranged as in the claim."

The Office Action states that the Behnke et al. patent teaches a dipstick immunodisplacement device and method where an analyte in a sample displaces

bound label from a specific binder bound to a solid phase, which is dipped into the vessel containing the sample. However, when read more specifically, the Behnke et al. patent discloses a much more complicated process. As set forth in column 5, lines 20-33, the process involves taking a test solution that contains a sample and another reaction partner and putting the solution in contact with one end of a test strip. The test solution is allowed to pass over at least one part of the test strip, including the partial area containing the antibody, by capillary migration. The test strip is subsequently washed and the test strip is brought into contact with a developing solution that contains members of a signal-generating system that are able to generate a detectable signal as a function of the amount of analyte in the sample and the partial area containing the antibody. This is in contradistinction with the method of the presently pending claims, which instead do not require a washing step. It was previously thought by those of skill in the art that washing was required in order to stop the reaction; i.e., stopping the biological activity of the bioactive molecule and also to remove any unbound ligand. The presently pending claims, therefore, are beneficial over the prior art in that they are able to remove the washing step and thereby simplify the assaying procedure. Since the Behnke et al. patent does not disclose the method of the presently pending claims, the claims are patentable over the Behnke et al. patent and reconsideration of the rejection is respectfully requested.

Claims 1-21 stand rejected under 35 U.S.C. §103(a) as obvious over the combined teaching of the Marquardt et al., Eibl et al., Fish et al., and Köhler patents. Reconsideration of the rejection under 35 U.S.C. §103(a) over the Marquardt et al., Eibl et al., Fish et al., and Köhler patents, as applied to the claims is also respectfully requested.

The Office Action states that the Marquardt et al. patent teaches solid phase assays, both competitive and non-competitive, for bioactive substances, including enzymes and their inhibitors, essentially as instantly disclosed except for being performed in microtiter plates rather than on an insertable solid phase. However, as set forth in the present specification on page 2, lines 24-30, the method of the Marquardt et

al. patent involves multiple steps including coating the wells of the microplate, washing the wells, adding biologically active substance to the wells, washing the wells once more, adding the indicator's enzyme to the wells, washing the wells again, and adding a colored development reagent. Therefore, this assay cannot be readily used in assays requiring rapid analysis and the method involves a multitude of steps as compared to the presently pending claims. Further, the Marquardt et al. patent requires a washing and development step. It is previously known to those of skill in the art that washing was required in order to stop the reaction; i.e., stopping the biological activity of the bioactive molecule and also to remove any unbound ligand. The presently pending claims are an improvement over the prior art in that they are able to remove the washing step and thereby simplify the assaying procedures. Therefore, the Marquardt et al. patent does not disclose the method of the presently pending claims.

The Office Action states that the Eibl et al. patent discloses elongated elements such as "platelets" or pins, which are secured to a holding band in a carrier and that are insertable into the recesses of a microtiter plate containing samples to be assayed. Further, the Office Action states that various competitive assay formats are taught using an antigen or antibody bound to the elements and a labeled antigen or antibody added to the sample. Therefore, the Office Action concludes that the Eibl et al. patent teaches the carrier for the avoidance of complicated separating and washing procedures as are found in prior art assays performed with coated vessels, such as tubes. It is undisputed that the Eibl et al. patent discloses the use of elements that are secured to a holding band in a carrier that is insertable into the recesses of a microtiter plate containing samples to be assayed. However, when read more specifically, the Eibl et al. patent teaches an assay that utilizes "a solution of the radioactively labeled antibody is added to the sample to be examined for a content of antigen or antibody, and then a solid carrier loaded with unlabeled antigen is contacted with the sample liquid, whereupon after washing the carrier, the radioactivity of the carrier is measured." This is specifically set forth in column 2, lines 28-33, of the Eibl et al. patent. In other words, the Eibl et al. patent teaches an assay kit, but still requires a washing step in order to measure the radioactivity of the carrier. While the Eibl et al. patent discloses an assay

kit with a decreased amount of steps required for performing the assay, it still requires washing procedures to be used in order for the assay to perform properly. This is in contradistinction with the method of the presently pending claims, which instead do not require a washing step. It was previously thought by those of skill in the art that washing was required in order to stop the reaction; i.e., stopping the biological activity of the bioactive molecule and also to remove any unbound ligand. The presently pending claims, therefore, are beneficial over the prior art in that they are able to remove the washing step and thereby simplify the assaying procedure. Therefore, the Eibl et al. patent does not disclose the method of the presently pending claims.

The Fish et al. patent, according to the Office Action, teaches the general use of coated comb-like carriers for assays to detect binding of a variety of receptor-analyte pairs, such as enzyme-substrate, antibody-antigen, antigen-antibody, receptor-toxin, receptor-drug, or complementary nucleic acid pairs. However, when read more specifically, the Fish et al. patent again requires a washing step as found in the above described prior art patents. Specifically, the card of the Fish et al. patent must be developed in order to determine the presence of an analyte in each of the samples. The card is washed and then immersed in a second compartment and any additional compartments. This developing step is not required by the present invention nor do the presently pending claims recite use of a card for conducting the assay. Therefore, the Fish et al. patent does not disclose the method of the presently pending claims.

Finally, the Office Action states that the Köhler patent teaches a comb-like carrier coated with antigens or antibodies for immunological assays as an alternative to coated microtiter plates, using a microtiter plate only as a vessel for multiple samples. However, the Köhler patent discloses in column 2, line 67 through column 3, line 6, that the strips are treated with a reagent in conjunction with naphthol, which is subject to a color change as a result of the immunological reactions. The reaction result can not otherwise be observed optically. Therefore, as with the above referenced prior art patents, there is a requirement that an additional washing or treatment step be performed in order for the assay to function properly. This is in contradistinction with

the assay and method of the presently pending claims, which instead require that no washing step be used. Therefore, the Köhler patent does not disclose the assay and method of the presently pending claims.

The Office Action concludes that it would be obvious to one of ordinary skill in the art, at the time the instant invention was made, to have substituted the comb-like carriers known in the art, as taught by the Eibl et al., Fish et al., and Köhler patents, for the microtiter plates in the assays of the Marquardt et al. patent because the Eibl et al., Fish et al., and Köhler patents teach these well-known carriers generally for the performance of a variety of assays. However, as detailed above, all of the cited assays require additional steps and there is no teaching nor suggestion in any of the prior art patents for the removal of a washing or treatment/development step for the assay to function properly. The present invention, therefore, improves upon the assays of the prior art by enabling the entire assay performance without requiring an additional washing or treatment/development step. Since none of the prior art patents alone or in combination teach nor suggest the method of the presently pending claims, reconsideration of the rejection is respectfully requested.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above. The prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In view of the present amendment and foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

KOHN & ASSOCIATES

Amy E. Rinaldo
Registration No. 45,791
30500 Northwestern Highway
Suite 410
Farmington Hills, Michigan 48334
(248) 539-5050

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 on April 26, 2002.

Angel Webb

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Page 2, second paragraph,

The pharmaceutical industry utilizes the methods mentioned above to screen compounds for discovering drugs. This process is slow due to the multiple steps required and the large amount of compounds needed to be tested. Typically, on a good day, a lab might test 100 to 1,000 compounds. However, in the race to commercialize, pharmaceutical manufacturers are facing great pressure to reduce the time required to discover new clinical drugs, cut assay costs, and screen more compounds and against more targets. Therefore, there is a very high demand to develop new methods to meet the requirements of High Throughput Screening (HTS). There has been described a method using quenched BODIPY dye-labeled casein as a substrate for determining the activities of protease, which is sensitive and amenable to automation (Jones, L.J. et al, 1997, *Anal Biochem* **251**:144-152). The degree of quenching of the fluorescent tag is crucial in this method. However, if there is not enough quenching due to poor conjugation or degradation of the fluorescence-labeled substrate under storage, etc. the assay will not be very useful. Also this procedure has relatively high background values which reduce its sensitivity. Another example of a potentially useful high throughput assay was made by Marquardt, et al and described in [PCT/]WO97/43438. The method involves many steps, including coating wells of a microplate, washing wells, adding biologically active substance to the wells, washing the wells once more, adding the indicator enzyme to the wells, washing the wells again, and adding a color development reagent. As a result, the assay cannot be readily used in assays requiring rapid analysis.

IN THE CLAIMS:

1. (Amended) A method for measuring [the] an activity or concentration of a biomolecule comprising:

providing a reaction vessel containing a sample, said sample including a biomolecule having a biological activity;

providing a probe coated with a reactant, said reactant being capable of interacting with the biomolecule;

adding a known quantity of a compound with a detectable label to the sample;

inserting the probe into the reaction vessel such that the biomolecule and the detectable label contact the reactant and interact with the reactant such that label is bound to the reactant;

removing the probe from the reaction vessel; and

measuring [the] a quantity of detectable label in the reaction vessel and/or on the probe, whereby the quantity of detectable label measures the activity or concentration of a biomolecule.

2. The method according to claim 1 wherein the probe has a shape selected from the group consisting of: pin[-like]; cone[-like]; cubiod; cylindrical; star-shaped; and spire-shaped.

12. A method for measuring [the] an activity or concentration of a biomolecule comprising:

providing a reaction vessel containing a sample, said sample including a biomolecule having a biological activity;

providing a probe coated with a reactant, said reactant being capable of interacting with the biomolecule, said reactant including a detectable label;

inserting the probe into the reaction vessel such that the reactant and detectable label contact the biomolecule and interact with the biomolecule such that label is released from the reactant;

removing the probe from the reaction vessel; and

measuring [the] a quantity of detectable label in the reaction vessel and/or on the probe, whereby the quantity of detectable label measures the activity or concentration of a biomolecule.

13. The method according to claim 12 wherein the probe has a shape selected from the group consisting of: pin[-like]; cone[-like]; cubiod; cylindrical; star-shaped; and spire-shaped.